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TITLE: Lung Injury; Relates to Real-Time Endoscopic Monitoring of Single Cells Respiratory Health in Lung

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**14. ABSTRACT**
The goal of this proposal is to design a portable bronchoscope that can determine the health status of the tracheal epithelial lining cells by analyzing changes in their metabolic profile. The device is intended to be used to quickly single out which individuals is showing injury and inflammation in the trachea and lung and therefore to provide them with the most adequate and early care. In this closing year 1 funding period, we have built the bronchoscope and done some preliminary testing on mouse trachea samples exposed to chemicals known to injure the tracheal epithelium. The size of the bronchoscope is quite small and will allow its transport and use by the military in the field or remote locations, while the small size of the instrument could permit its use on awake patients. Following evaluation of the field of research we have decided to develop a hybrid system Camera and Raster with two modalities: *seek* and *focus*. The former modality will allow low magnification scan of the trachea and lung airway to search for areas of interest that will then be analyzed in greater detail using the latter modality. Our preliminary data using tissue reflectance on mouse tracheal tissue have shown that our instrument can, indeed, successfully separate injured tracheal epithelial cells from the healthy ones without the use of additional reagents or chemicals.

**15. SUBJECT TERMS**
Lung injury, endoscopy, hyperspectral, spectraFLIM, fluorescence, autofluorescence, metabolic profile, non-invasive, basal cells, clara/club cells, SO2, naphthalene

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## INTRODUCTION:

Military personnel can be exposed by inhalation to dusts and toxicants in the field that may contribute to lung disease. The available technologies to detect early stage alterations of lung function in patients require a long processing time and lack satisfactory sensitivity and resolution. These existing medical technologies, can only visualize, but not precisely measure the metabolic health of individual airway lining cells. We will build and tune a new fiber-optic system that can be deployed alone or as a modification to an existing upper or lower airway scope instrument, that will detect airway lining cell injury with a greater specificity, sensitivity and speed.

**KEYWORDS:**

Lung injury, endoscopy, hyperspectral, spectraFLIM, fluorescence, autofluorescence, metabolic profile, non-invasive, basal cells, clara/club cells, SO2, naphthalene

## ACCOMPLISHMENTS:

### What were the major goals of the project?

**Subtask 1:** Evaluate sensitivity of Camera-SpectraFLIM

**Status:** Completed 2017-03

**Result:** We performed research enquiries on the actual sensitivity of current camera based tools for acquiring low intensity autofluorescent data. We evaluated the latest generation camera sensors designed by PCO AG GmbH (Kelheim, Germany) with frequency domain 40MHz rate and highest quantum efficiency peak on the market (39%@peak). After discussing with multiple industry developers and with the university research laboratory that spearheaded that product application[1], we concluded that, as of March 2017, this camera based technology is not mature for measuring autofluorescence. However, in our further researches we found that recent snapshot hyperspectral camera sensors (reflectance based), that use super-bayer filter technology, has reached a sufficient sensitivity for our application. We have chosen one of these cameras by PhotonFocus (Lachen, Switzerland) to pair with wide-field bronchoscopic observation.

**Milestone # 1:** Selection of optimal acquisition modality between Camera- and Raster-SpectraFLIM to be used in Aims 2-3

**Status:** Completed 2017-03

**Result:** After careful consideration we decided to develop a hybrid system Camera and Raster with two modalities: *seek* and *focus*. *Seek* modality is a large field, camera-based reflectance hyperspectral, that provides an intermediate accuracy for measuring lung injuries. This modality is coupled with a standard bronchoscope and already greatly enhances its capabilities. It acquires the reflectance spectrum of lung tissues and provides an intermediate accuracy result on tissue health using Hyperspectral Phasor analysis. Experimental results using this modality are reported below. Areas of interest with a higher likelihood of lung injury will be imaged using the *focus* modality, that provides high accuracy on a small field of view. This modality uses Raster scan SpectraFLIM to acquire autofluorescence, coupled with high efficiency GRIN lenses mounted on high density optical fiber bundles.

**Subtask 2:** Implement SpectraFLIM onto Bronchoscope and calibrate with standards

**Status:** 80% complete

**Result:** Two acquisition modalities are to be implemented on the instrument: *seek* and *focus*. *Seek* modality utilizes snapshot reflectance hyperspectral imaging combined with HyperSpectral Phasor. This modality has been implemented on a bronchoscope using low profile camera (Figure 1).

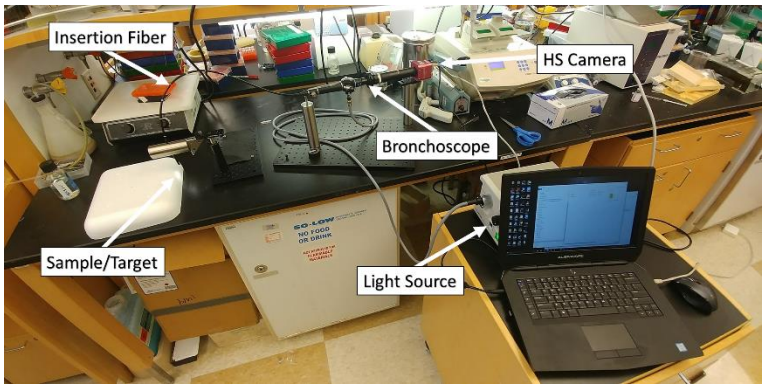



**Figure 1**: *Seek* modality setup for snapshot Hyperspectral Phasors reflectance. Endoscopic light source provides excitation spectrum between 400nm and 800nm. Bronchoscope fiber delivers excitation light and collects reflected light directed to a low profile hyperspectral camera mounted on distal side of bronchoscope. Data is processed using HySP software.

*Focus* (Figure 2) modality is still under implementation, currently has scanning unit, laser filters, electronics controllers, imaging fiber bundles with GRIN lens. All these components are custom designed and made.

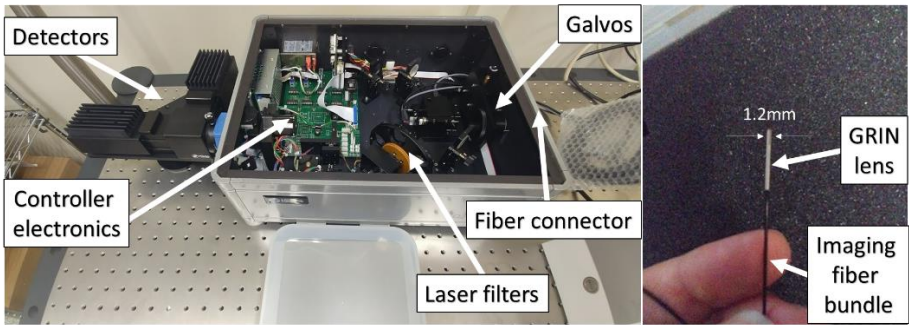



**Figure 2**: *Focus* modality prototype setup for SpectraFLIM measurements. Laser filters sort excitation light to be raster scanned using Galvos onto an imaging fiber bundle. This fiber bundle contains 30k fibers and is factory fused to a GRIN lens that will focus light onto the sample. The small diameter of the lens allows access to the auxiliary port of a bronchoscope like the one in used in *Seek* modality.

**Subtask 3:** Submit IACUC Protocol for animal testing

**Status:** Completed 2017-01

**Result:** IACUC Protocols were drafted, submitted 2017-01. Minor amendments for transport of samples from Children's Hospital Los Angeles to USC University park campus were submit 2017-08.

**Milestone # 2:** SpectraFLIM implemented onto Bronchoscope and calibrated

**Status:** 80%

**Result:** Design of SpectraFLIM unit was prepared, optimized and submitted to manufacturers. Some custom components required longer than expected for fabrication and assembly. Expected delivery for the last components is approximately 1 month.

**Milestone #3**: Approval of IACUC protocol

**Status:** Completed 2017-03

**Result:** IACUC Protocols were approved by USC Board in 2017-03. Minor amendments for transport of samples from Children's Hospital Los Angeles to USC UPC were accepted 2017-09.

**Subtask 4:** Pilot study SO2 and diphtheria toxin (8-20 mice)

**Status:** 75%

**Result:** We performed pilot studies on mice with naphthalene and SO2 using the Seek modality setup. Experiments allowed optimization of protocols for both image acquisition and sample preparation.

- The Naphthalene exposure protocol we used, efficiently depleted the Club cells in the tracheal epithelium. The loss of the Club cells was more prominent in the distal portion of the trachea (closer to the bronchi).
- To expose animals to SO2 gas we created a propylene exposure chamber to deliver SO2 (500ppm) mixed in 80% N2/20% O2 to the animals. Histological analysis showed marked loss of the tracheal Clara and ciliated cells at 1 and 3 days post exposure. The tracheal epithelium completely regenerately by around 7 days post injury.
- The last injury model entails the expression of the diphtheria toxin specifically in the lung basal cells using the KRT-5ER-CRE mouse transgenic line: the breeding and the testing of these animals have been delayed of about 2 months. This was caused by the necessity to write a full new IACUC protocol to allow the transport of animals from CHLA to USC UPC to facilitate some of the tissue imaging procedures.

**What was accomplished under these goals?**

1) major activities

1a) **Technology landscape assessment**: we performed a thorough analysis of currently existing technology both available commercially and in developmental stage. Performed meetings with multiple leader manufacturers in the field of:

- detectors: we compared Hamamtsu Photonics K.K., Hamamatsu City, Japan; Leica Microsystems, Wetzlar, Germany; Gpixel Inc, Changchun, China; Spectral Devices Inc., London, Canada.
- Optomechanics: we compared Optics Technology Inc, Pittsford, NY; ISS, Urbana-Chamapign, IL; Mirrorcle Technologies Inc, Richmond, CA.
- fiber optics and lenses: we compared Grintech Gmbh, Jena, Germany; Tag Optics Inc., Princeton, NJ; Mitsubishi Cable America Inc., Blue Bell, PA; Fujikura Ltd, Tokyo, Japan; US Fiberoptec Technology Inc, San Jose, CA.

1b) **Instrument design**: based on the information obtained through assessing the technological landscape we designed a hybrid raster scanning SpectraFLIM and

snapshot reflectance hyperspectral system, *seek* and *focus* (described in milestone #1 above). This system leverages existing technology for bronchoscopy to gain access into airways and exploits auxiliary bronchoscope port to insert a custom made optical fiber bundle factory coupled to a medical grade gradient index objective.

1c) **Building and calibration**: we assembled the Seek modality of the instrument, that provides an intermediate lung injury assessment accuracy on a large field of view, utilizing low profile camera-based reflectance hyperspectral (Figure 1).

1d) **Preliminary testing on mice**: we performed 4 sessions of iterative optimization for injury protocol and experimental imaging. During this we performed injury assessment of lung airways of mice exposed to naphthalene and SO2 as well as control animals.

2) specific objectives

The objective of this first year was to design and establish an instrument and experimental pipeline for performance assessment thorough experimentation in year 2.

In summary:

2a) We evaluated sensitivity of Camera based approaches for measuring SpectraFLIM

2b) We designed an instrument that hybridizes Camera hyperspectral reflectance with Raster SpectraFLIM

2c) We implemented Seek modality on a bronchoscope and performed calibration with standards

2d) We submitted IACUC protocols and obtained approval

2e) We performed pilot studies of SO2 and naphthalene lung injuries

3) significant results or key outcomes, including major findings, developments, or conclusions (both positive and negative)

3a) Significant Results: from preliminary experiments, lung injuries appear to have characteristic phasor signatures depending on the chemical used and the location of lung epithelial injury. Different positions in the lung are affected in different ways by chemicals. Preliminary assessment shows phasor differences in these lung positions (Figure 3,4).

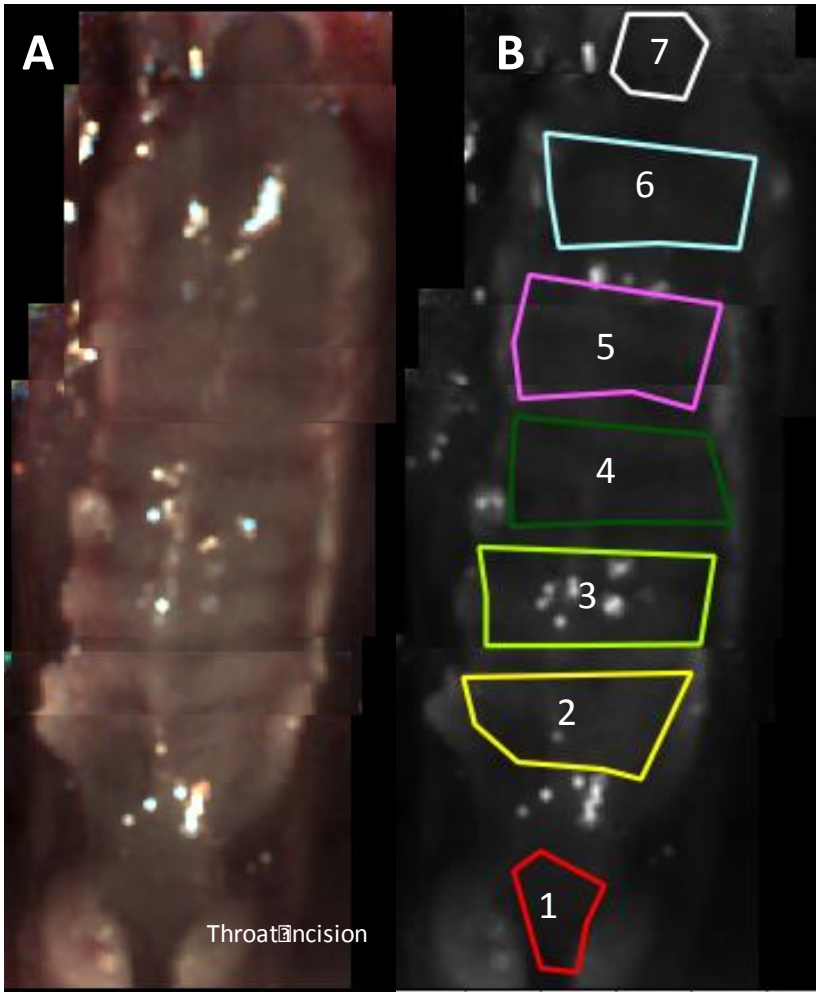



**Figure 3**: Preliminary results for *Focus* modality SpectraFLIM measurements. During experimental procedures we developed an analysis pipeline. Data is first acquired as separate hyperspectral images as a "fly-over" on an open mouse throat incision (A). Using the position of trachea (B,7) we create a series of ROI for performing analysis. With an approximately constant pixel size we repeated the analysis on multiple mice with different injuries to have a comparison of phasor signatures at different positions in the airways.

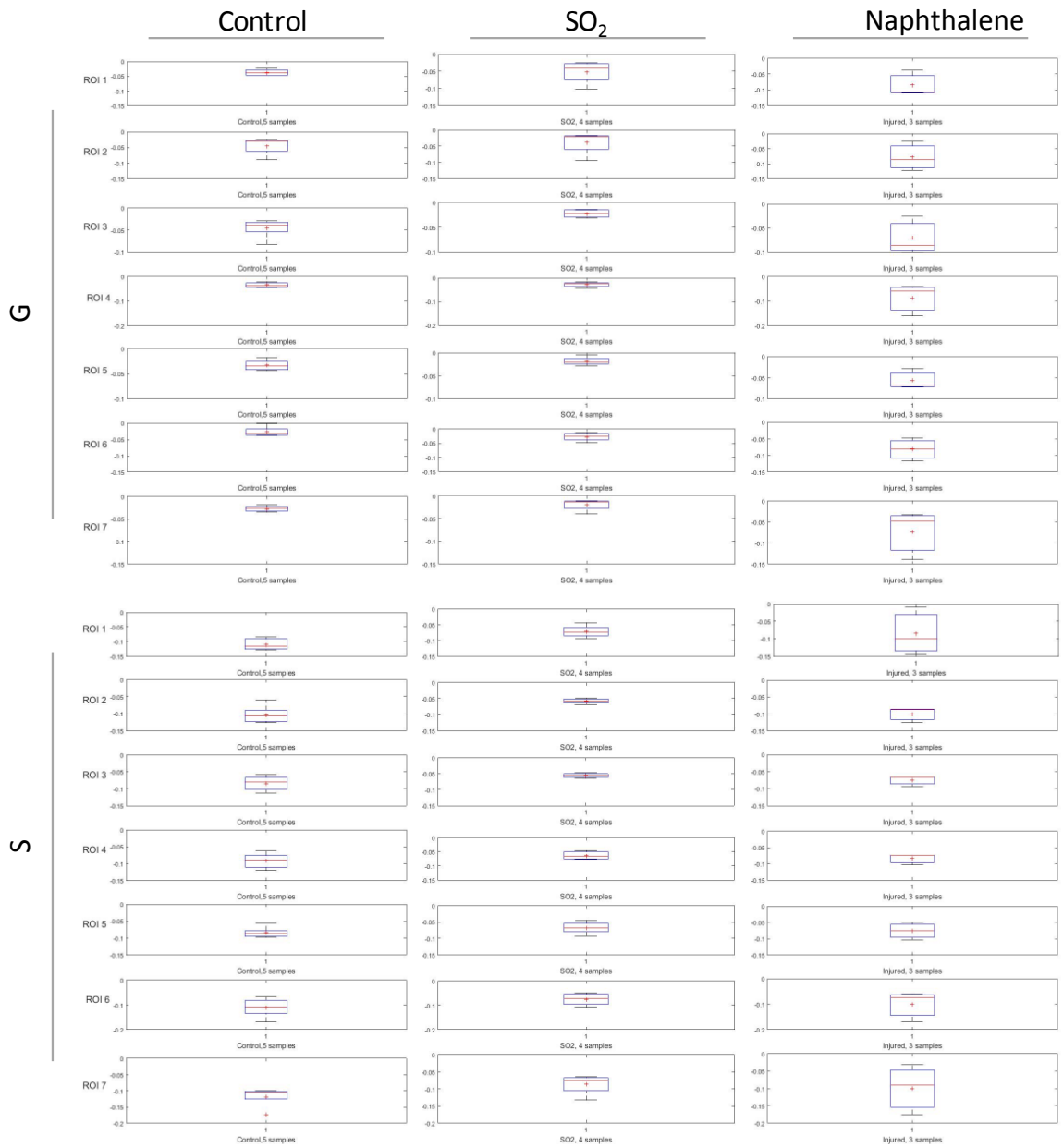


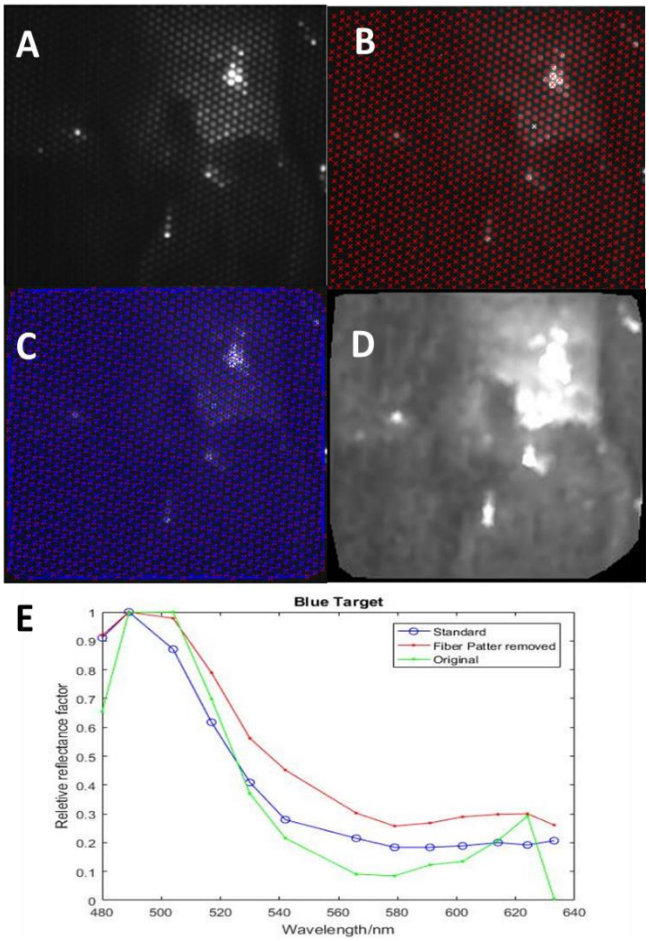

**Figure 4**: Preliminary results for *Focus* modality SpectraFLIM measurements. In this large map we report the preliminary results in terms of G and S coordinates of the phasor plot. The box plots represent mean (+), median (red line), minimum and max values as well as standard deviation (box) over multiple samples. The experiment was repeated on control samples and samples exposed to SO2 as well as naphthalene. The plots show significant differences for the 3 samples, suggesting each injury has a specific phasor pattern. For each ROI selected in figure 3, we perform phasor analysis and characterized the average phasor coordinates of that region. Interestingly the regions closer to trachea (ROI 7) exhibit smaller differences compared to ROIs deeper in the lungs. This is an expected result as this injury is expected to be stronger in deeper positions in lungs (ROI1).

3b) Development: Seek modality can be used as an intermediate assessment tool for determining areas of interest to be imaged with SpectraFLIM in greater detail.

3c) Technical assessment conclusion: After discussing with multiple industry developers and several university research laboratories that tested similar sensitivity applications we concluded that, as of March 2017, camera based technology is not mature for measuring autofluorescence. However, camera based snapshot hyperspectral technology is a viable instrument for measuring reflectance hyperspectral.

4) other achievements

4a) Developed a **fiber pattern correction for hyperspectral imaging** based on Delaunay triangulation. During our preliminary testing using Hyperspectral Phasors in combination with a commercial bronchoscope we observed presence of fiber patterns in the image. Multiple algorithms have been presented in literature for "color" and "monochrome" fiber pattern correction. However, no algorithm has been presented yet that can correct these fiber patterns in combination with hyperspectral data acquisition (Figure 5 (left) and 6 (below). We are currently testing the algorithm performance and limits in preparation of a scientific manuscript.



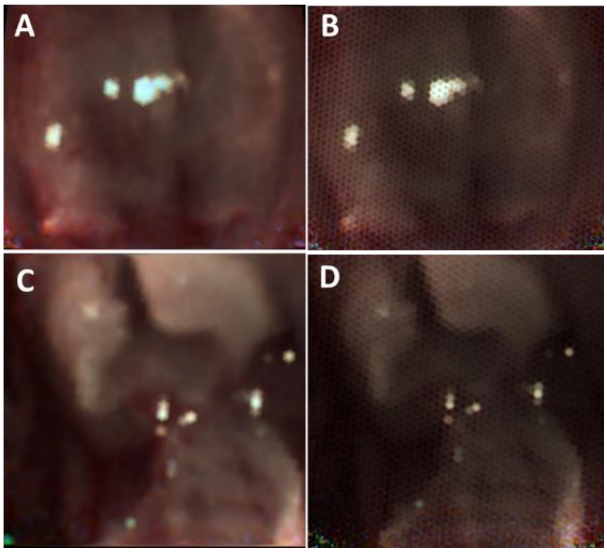




**Figure 5**:Hyperspectral fiber pattern correction algorithm. This preliminary result shows application of a novel algorithm that corrects patterns on the image resulting from fiber bundles (A) while maintaining good confidence on spectral information. Steps for pattern removal involve fiber detection (B), hyperspectral Delaunay triangulation (C) and corrected image (D). The advantage and novelty of this approach is the close confidence in spectral domain information when snapshot hyperspectral images are acquired. (E) shows comparison spectra acquired using a calibrated blue target. The reference calibrated spectrum is represented in (green); before fiber pattern removal data is represented in (blue). After fiber pattern removal is represented in (red). Removal process fits within 10% error of raw data, outperforming in the lower and higher wavelengths the standard and approximating values closer to the original.

**Figure 6**: Example application for Hyperspectral fiber pattern correction algorithm. This example shows the result of such algorithm applied hyperspectrally and represented as a "color" image. A) corrected image of mouse airway from corresponding B) raw image with honeycomb pattern. Similarly C) shows a hyperspectrally corrected mouse trachea, reconstructed from pattern D) raw image.

4b) **Compressive spectral algorithm (Phasor-Maps)**: in order for us to understand the health status of the lungs, we need to perform accurate analysis. The *seek* and *focus* strategy places the accurate analysis in a specific region of interest identified during *seek*. However, we foresee a time limitation in how long a doctor or medic can spend seeking these regions of interest. For this purpose, we have developed a compressive spectral algorithm that represents, using special color maps (Phasor-Maps), the spectral dimension as a color. Differently from remote sensing approaches, our approach is directed at enhancing and highlighting spectral differences, from very subtle to very wide, for spectra with different Fourier phase and magnitude. A scientific manuscript about this is in preparation.

SpectraFLIM implementation on a bronchoscope has been completed at 80%. The reason behind this delay is the amount of custom components we needed for this setup. In particular fiber systems, spectral and lifetime were designed by us and custom made at factory. Delivery is expected in approximately one month.

1- Diphtheria toxin experiments: the use of the diphtheria toxin was described in the amendment 2 to the protocol 386-16 (CHLA). The same amendment also requested the transport of animals from CHLA to USC UPC to facilitate tissue imaging described in year 2. To receive animals, USC requested a new mouse protocol (USC mouse protocol 20685 which mirrored the CHLA 386-16), an amendment to add Dr. Turcatel to work with mice at USC UPC and a signed MOU document. Furthermore, Dr. Turcatel had to attend and retrain on all the USC IACUC training courses. This process halted the approval of the amendment 2 describing the diphtheria toxin injury model until late August 2017. Therefore, the diphtheria toxin injury experiments have been delayed for around 2 months and will be performed in October-November 2017. However, this postponement won't affect the overall project as subtask 4 (obtaining standard of phasor for positive diphtheria toxin) was originally planned to be accomplished in the second half of the second year (18-24 months).

**What opportunities for training and professional development has the project provided?**

This project created great opportunities for training and professional development both for key personnel and students involved in the work. Two students received mentoring, one key personnel developed mentoring skills.

One USC master student, Mr. Pu Wang, had the chance to greatly improve his knowledge in hyperspectral imaging and camera programming, as well as learning how a translational project

can be designed, tested and optimized. This opportunity resulted in one novel fiber pattern correction and one manuscript in preparation.

One graduate student also received mentoring, Ms. Wen Shi, where she acquired deep knowledge of the phasor analysis and aided in the development of novel visualization algorithms and performed experiments. This mentoring resulted in one novel compressive algorithm and one manuscript in preparation.

One key personnel, Dr. Francesco Cutrale, had the chance to mentor the students and attain a greater proficiency in performing one-on-one mentoring with a clear project, target and results.

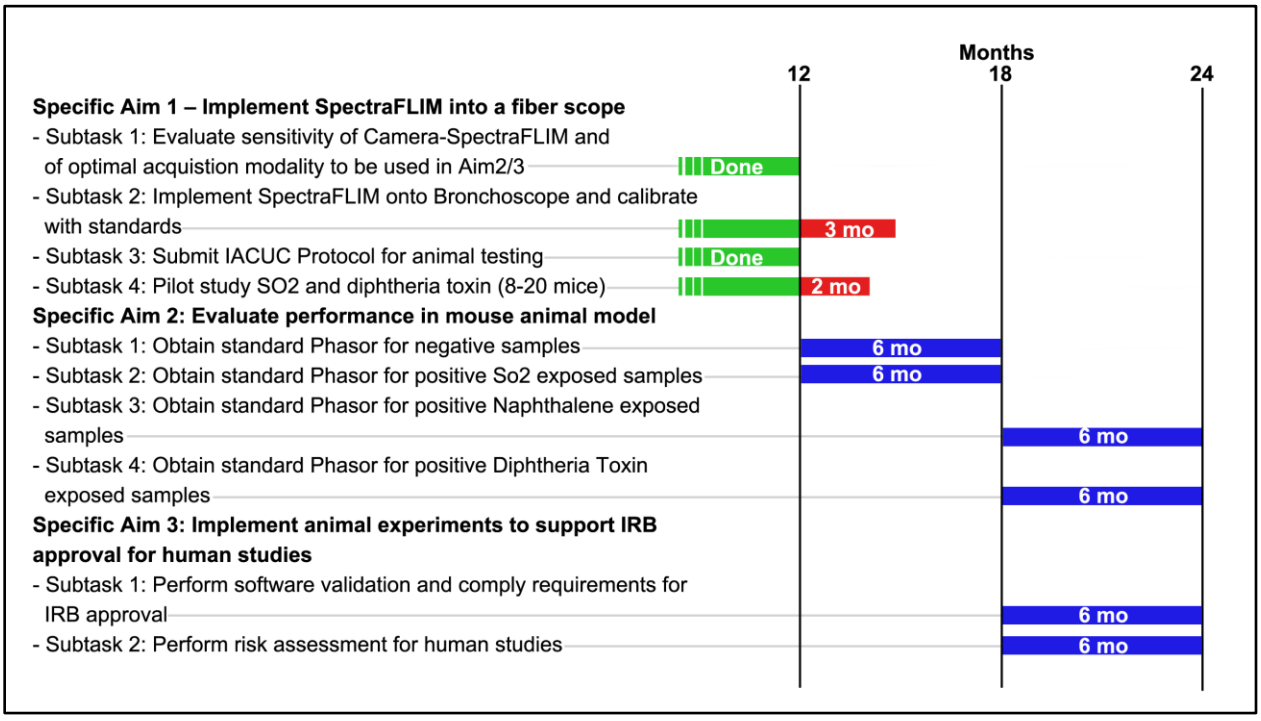
**How were the results disseminated to communities of interest?**

Results were disseminated at the "Unraveling Vascular Inflammation: From Immunology to Imaging" Conference organized by National Heart, Lung, and Blood Institute, NIH, DHHS in Bethesda, MD. During this meeting a poster was presented with preliminary results, receiving particular interest by the prevalently MD crowd.

Results were also presented at a Children's Hospital Los Angeles retreat organized in Pasadena, CA where the method and purpose in this work were reported to a mixed group of scientists and medical specialists.

**What do you plan to do during the next reporting period to accomplish the goals?**

To accomplish all the goals and objectives for the next reporting period we will make sure we're on schedule with our Gantt chart (below)



**IMPACT:**

**What was the impact on the development of the principal discipline(s) of the project?**

The main techniques that were developed in this first year of funding explore the dimension of color using hyperspectral imaging. We assembled a portable instrument capable of acquiring multidimensional images of the lungs in either humans or animals. The preliminary experiments we perform suggest that lung injuries appear to have characteristic phasor signatures depending on the chemical used and the location of lung epithelia injury. Identifying these phasor signatures will move us one step closer to noninvasively and quantitatively classifying lung injuries.

During the development of the main instrument, we also created novel algorithms aimed for biomedical imaging but, truly, applicable to a large variety of fields. Looking through a fiber bundle produces a characteristic pattern that reduces the quality of the image. Multiple approaches have been proposed in literature for correcting this pattern. However, no algorithm is available that can perform this task in hyperspectral or multi-dimensional images. We developed an algorithm that combines Delaunay triangulation, pattern removal and hyperspectral imaging that improves the quality of data while maintaining the spectral information. This work is likely to result in Intellectual Property filing, one publication is currently being drafted.

Another technical advance is a compressive algorithm for multidimensional data, that can visualize hyperspectral and lifetime datasets as a “color” image while enhancing the hyperspectral content information. This algorithm is also generic and can be applied to different fields of compressive sensing. It utilizes special color maps that evolve from Fourier-phasor approach, which we named Phasor-maps. We are preparing IP disclosure in parallel to a technical scientific manuscript.

**What was the impact on other disciplines?**

Nothing to report

**What was the impact on technology transfer?**

The project is likely to produce 2 IP disclosures within the first year of funding. We anticipate interest from industry for these algorithms, particularly in the field of medical imaging. We are currently designing a business model for initiating a start-up company based on IPs translating from this project.

**What was the impact on society beyond science and technology?**

Nothing to report

## CHANGES/PROBLEMS:

### Changes in approach and reasons for change

Nothing to report

### Actual or anticipated problems or delays and actions or plans to resolve them

1- SpectraFLIM implementation on a bronchoscope has been completed at 80%. The reason behind this slight delay is the amount of custom components we needed for this setup. In particular fiber systems, spectral and lifetime were designed by us and custom made at factory. Delivery is expected in approximately one month.

2- The diphtheria toxin pilot experiments have been delayed for about 2 months. This was caused by the necessity to write and obtain approval for a new IACUC protocol that allowed the transport of animals from CHLA to USC UPC. We plan to perform these tests in October-November 2017. This delay, as also explained above, won't materially affect the over-all project timing as the diphtheria toxin injury model will be used in the second part of the next reporting year (see original statement of work and Gannt chart), which will give us ample time to tune up the injury models.

### Changes that had a significant impact on expenditures

Nothing to report

### Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Nothing to report

**PRODUCTS:**

**Publications, conference papers, and presentations**

Multi-modal fluorescence as an insight tool for imaging vasculature; Francesco Cutrale, Cosimo Arnesano, Le A. Trinh, Gianluca Turcatel, David Warburton, Scott E. Fraser; Poster; Unraveling Vascular Inflammation: From Immunology to Imaging Conference; National Heart, Lung and Blood Institute, NIH, DHHS

Enhancing visualization of hyperspectral data with Phasor-Maps; Wen Shi, Eun Koo, Le A. Trinh, Benjamin Steventon, Scott E. Fraser, Francesco Cutrale; Poster; American Society of Cell Biology (ASCB) Meeting 2017

**Journal publications**.

Nothing to report

**Books or other non-periodical, one-time publications.**

Nothing to report

**Other publications, conference papers, and presentations.**

Nothing to report

**Website(s) or other Internet site(s)**

Nothing to report

**Technologies or techniques**

Nothing to report

**Inventions, patent applications, and/or licenses**

The project is likely to produce 2 IP disclosures within the first year of funding. IP disclosures are under preparation for:

- hyperspectral fiber pattern removal algorithm
- compressive spectral algorithm (Phasor-maps)

## Other Products

During the first year of this project we report the following research tools:

**Software:**

- Hyperspectral fiber pattern correction: improves hyperspectral imaging when performed through a fiber bundle
- Compressive spectral algorithm (Phasor-Maps): compresses spectral information for fast visualization that enhances different types of spectral differences

**Instruments or equipment**:

- Seek Hyperspectral Bronchoscope: Phasor powered system capable of interfacing with existing bronchoscopes and acquiring hyperspectral reflectance data of wide areas for identifying areas of interest to be imaged with SpectraFLIM.
- Focus SpectraFLIM system: system has been designed and is in its final stage of assembly.

## PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

### What individuals have worked on the project?

| | |
|---|---|
| Name: | David Warburton |
| Project Role: | Project Director/Principal Investigator |
| Researcher Identifier (ORCID ID): | 0000-0002-4605-1298 |
| Nearest person month worked: | 1.26 calendar months |
| Contribution to Project: | Dr. Warburton is the PI of this project and is responsible for coordinating the overall project and making sure that milestones are met. |
| Funding Support: | DOD, NIH, CHLA |

| | |
|---|---|
| Name: | Rex Moats |
| Project Role: | Key Collaborator / CHLA |
| Researcher Identifier (ORCID ID): | 0000-0002-5448-6988 |
| Nearest person month worked: | 1.20 calendar months |
| Contribution to Project: | Dr. Moats is responsible for coordinating the biological with the imaging aspects of the project. |
| Funding Support: | DOD, NIH |

| | |
|---|---|
| Name: | Gianluca Turcatel |
| Project Role: | Key Collaborator / CHLA |
| Researcher Identifier (ORCID ID): | 0000-0002-4178-5081 |
| Nearest person month worked: | 5.04 calendar months (09/01/16 – 06/30/17)<br>0.20 calendar months (07/01/17 – 08/31/17) |
| Contribution to Project: | Dr. Turcatel wrote the mouse protocol and amendments and led the communication between CHLA and DOD regarding the use of animals for experimentation. He purchased the transgenic animals and bred them to obtain the desired genotype. He performed the genotyping of the pups for each offspring. He designed and tested the SO2 exposure chamber to selectively injure the tracheal epithelium. He performed the injury experiments (naphthalene injection and SO2 exposure), collected the tracheal tissue and performed the histological analysis. |
| Funding Support: | DOD, American Heart Association |

| | |
|---|---|
| Name: | Scott E. Fraser |
| Project Role: | Principal Investigator / USC |
| Researcher Identifier (ORCID ID): | 0000-0002-5739-4026 |
| Nearest person month worked: | 1.20 calendar months |

| | |
|---|---|
| Contribution to Project: | Dr. Fraser has overseen the SpectraFLIM project, providing solutions and suggestions on innovative options for performing this Translational Microscopy. He helped designing the SpectraFLIM microscope setup, choice of hardware. He contributed designing experiments. |
| Funding Support: | DOD, NIH, University of Southern California internal funding |
| Name: | Francesco Cutrale |
| Project Role: | Key Collaborator / USC |
| Researcher Identifier (ORCID ID): | 0000-0003-0517-3069 |
| Nearest person month worked: | 6.00 calendar months |
| Contribution to Project: | Dr. Cutrale is the expert in Hyperspectral Phasors and Multispectral Imaging Microscopy. He helped designing the SpectraFLIM microscope setup, choice of hardware and performing extensive market research for evaluating devices for hyperspectral acquisitions. He designed experiments for bronchoscope imaging and performed the experiments. He wrote software for analysis, has overseen experimental analysis pipeline and mentored two students on parts of this project, particularly Hyperspectral fiber pattern correction and Compressive Spectral algorithm. |
| Funding Support: | DOD, University of Southern California internal funding, University of Southern California Coulter Foundation. |
| Name: | Cosimo Arnesano |
| Project Role: | Key Collaborator / USC |
| Researcher Identifier (ORCID ID): | 0000-0002-8843-2961 |
| Nearest person month worked: | 6.00 calendar months |
| Contribution to Project: | Dr. Arnesano is the expert in Fluorescence Lifetime Imaging Microscopy. He helped designing the SpectraFLIM microscope setup, choice of hardware and performing extensive market research for evaluating devices for FLIM acquisitions. He contributed designing experiments for bronchoscope imaging and performing the experiments. |
| Funding Support: | DOD, NIH, University of Southern California internal funding |

| | |
|---|---|
| Name: | Wen Shi |
| Project Role: | Graduate Student |
| Researcher Identifier (ORCID ID): | 0000-0002-6624-2331 |
| Nearest person month worked: | 6.00 calendar months |
| Contribution to Project: | Ms. Shi has contributed coding and development for the Compressive Spectral Algorithm (Phasor Maps) under the mentorship of Dr. Cutrale. She optimized algorithms for compressive visualization of data in close-to-realtime. |
| Funding Support: | University of Southern California internal funding |

| | |
|---|---|
| Name: | Pu Wang |
| Project Role: | Master Student |
| Researcher Identifier (ORCID ID): | 0000-0002-8664-6886 |
| Nearest person month worked: | 3.00 calendar months |
| Contribution to Project: | Mr. Wang has contributed coding and development for the hyperspectral camera under the mentorship of Dr. Cutrale. He contributed calibration of the bronchoscope system as well analysis of data. |
| Funding Support: | University of Southern California internal funding, University of Southern California Coulter Foundation. |

**Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?**

Dr. David Warburton – Nothing to Report

Dr. Rex Moats – Nothing to Report

Dr. Gianluca Turcatel – Dr. Turcatel has been promoted to Assistant Professor and received an American Heart Association grant.

AHA Reference Number – 17SDG33670959
Title – Tgf-beta signaling pathway induces gender specific phenotype in embryonic murine lung
07/01/2017 – 06/30/2020
4.20 calendar months

Dr. Scott E. Fraser – Nothing to Report

Dr. Francesco Cutrale – Nothing to Report

Dr. Cosimo Arnesano – Nothing to Report

**What other organizations were involved as partners?**

USC is a leading private research university located in Los Angeles, CA since 1895. The Keck School of Medicine at USC has been affiliated with Children's Hospital Los Angeles since 1934. The faculty of USC staffs both the university and the hospital. Dr Fraser is the Provost Professor at USC. His laboratory is located in a purpose built Convergent Imaging Sciences building on the University Park Campus adjacent to the Coliseum. Dr Warburton the PI of this project is a tenured and endowed Professor of Pediatrics, Surgery and Craniofacial Biology at USC and directs a large Developmental Biology and Regenerative Medicine Research Program at the Saban Research Institute, which is located at CHLA in Hollywood, CA. These campuses of USC are connected by high bandwidth ecomms. Drs Warburton, Moats and Fraser communicate weekly either in person or on ecomms and there is a monthly in person all hands grant progress coordination meeting at Saban.

Organization Name: University of Southern California

Location of Organization: Los Angeles, CA

Partner's contribution to the project (identify one or more)

- Facilities
- Collaboration
- Personnel exchanges

**SPECIAL REPORTING REQUIREMENTS**

**COLLABORATIVE AWARDS:** Not Applicable

**QUAD CHARTS:** Not Applicable

**APPENDICES:**

Nothing to Report